Substitute Specification - Marked-Up Copy

CoQ_{10}-CONTAINING PRELIPOSOMES AND PREPARATION THEREOF

~~containing preliposomes and preparation thereof~~

Field of the ~~Of The~~ Invention

The present invention relates to the fields ~~field~~ of ~~Pharmaceutics~~ pharmaceutics and ~~cosmetic,~~ cosmetics. More specially, the present invention relates to CoQ_{10}-containing preliposomes, and more particularly, ~~in particular,~~ relates to the preparation method and the application of CoQ_{10}-containing preliposomes which ~~contains~~ contain spongiamine.

BACKGROUND of the ~~Of The~~ Invention

CoQ_{10} (conenzymeQ_{10}, ubidecarenone) is a kind of a liposoluble quinine compound, which has the same character as a ~~with~~ vitamin. The ~~prominence~~ prominent function of CoQ_{10} is anti-oxidation and ~~to clean the~~ cleaning free ~~radicals,~~ radicals. CoQ_{10} is one of the most important functional components used in many anti-aging products at present. It ~~is~~ has been proved experimentally ~~by the experiment~~ that CoQ_{10} can accelerate the metabolism of ~~the~~ skin, accelerate the transport of cellular respiration chain and ~~the~~ ATP production of facial and hand skin. ~~the skin of face and hand. Simultaneity,~~ Simultaneously, CoQ_{10} can inhibit ~~the peroxide~~ oxidation of the skin lipid, and consequently nourish and activate the skin. It is reported that ~~the~~ body slimming ~~lotion~~ lotions and UV expert ~~cream~~ creams which

~~contains~~ contain CoQ_{10} ~~has~~ have obvious ~~effect~~ effects on preventing the formation of furrows, whitening the complexion, ~~increaseing~~ increasing the elasticity of the skin and so on. CoQ_{10} not only ~~protect~~ protects the skin, but also ~~prevent and cure the~~ prevents and cures skin diseases of ~~the~~ human beings. ~~being.~~ It ~~is proved by the experiment~~ has been experimentally proven that CoQ_{10} has obvious therapeutic ~~effect~~ effects on photoallergy, dermatitis, hair-lose, ~~bedsore, ulcer and woundof~~ bedsores, ulcers, wounds of the skin, hyperpigmentation and so on. ~~As~~ Because the molecular structure of CoQ_{10} has an unsaturated double bond, CoQ_{10} is extremely unstable and is easy to ~~be oxidated~~ oxidize and becomes decomposed by the oxygen and light in the ~~air,~~ ~~and~~ air. In addition, heating or contacting CoQ_{10} with metal ~~ion~~ ions will accelerate its decomposition. ~~it to be decomposed.~~ As a result, the content of CoQ_{10} in ~~the product has~~ products becomes decreased, ~~or~~ and the activity of CoQ_{10} ~~lost quickly, then affect~~ is quickly lost, adversely affecting the quality and actual effect of the products. ~~product.~~ In addition, CoQ_{10} is a liposoluble compound, which makes it difficult to mix ~~will result in difficulty in mixing~~ with the ~~water-solubility~~ water-soluble cosmetics. ~~cosmetic.~~ The foregoing disadvantages of CoQ_{10} extremely restrict the development and application of CoQ_{10}.

Liposomes are ~~Liposome is~~ composed ~~by~~ of hydrophilic bursa ~~bubble~~ bubbles which ~~consists with~~ consist of lecithoid double molecular layers. ~~layer.~~ Liposomes have characteristics that ~~Liposome has the character to~~ improve the stability of drug encapsulation, facilitate the percutaneous absorption of drugs, ~~the drug,~~ prolong the time of drug action, control the drug targeting at ~~the~~ local pathological ~~changes part~~

parts of the body, and decrease the side effects of drugs. ~~effect of the drug.~~ Thus, as drug carriers, liposomes have ~~drug carrier, liposome has~~ been widely used in pharmaceutics and cosmetics. ~~Pharmaceutics and cosmetic.~~ CoQ_{10} liposomes could improve the stability of drugs, ~~the drug,~~ facilitate the percutaneous absorption of drugs, ~~the drug,~~ and increase the water-solubility of drugs. ~~the drug.~~ But generally being a kind of liposome ~~liposomes~~ suspension solution, CoQ_{10} has obvious shortcomings in the stability. The reasons are as following:

1. As colloidial particulates, liposomes are ~~colloid particulate, liposome is~~ a kind of unstable thermodynamic system ~~thermodynamics instability system,~~ which is easy to congregate, fuse and sedimentate, and the oxidation decompose of the lecithoid causes ~~lecithoid,~~ leakage of the encapsulation drug ~~in~~ into the ~~water,~~ aqueous solution, etc., ~~will result~~ resulting in the instability of the liposome.

2. The instability of the structure of CoQ_{10} ~~will make the drug~~ makes drugs more instable in the water.

3. The ratio of CoQ_{10}, liposome suspension and ~~the~~ drug content is generally fixed; however, the required content of CoQ_{10} differs in different cosmetics. Thus, it is not convenient to mix CoQ_{10} liposome ~~suspension~~ suspensions with ~~cosmetic~~ cosmetics which contain ~~contains~~ CoQ_{10}.

So it is necessary to find a kind of liposome ~~prescription~~ preparation which is convenient, flexible, easy to mix with ~~cosmetic~~ cosmetics which contain ~~contains~~ CoQ_{10}, in order ~~able~~ to make the ~~liposome and drug~~ liposomes and drugs more stable, and ~~able to be stored~~ storable for ~~a~~ long periods of time.

Disclosure of the Invention ~~The description of the invention~~

~~The~~ An object of present invention is to overcome the shortcomings of CoQ_{10} and common CoQ_{10} liposome, and to supply a kind of CoQ_{10}-containing preliposomes which contain ~~contains~~ spongiamine. The present invention ~~could~~ will increase the stability of CoQ_{10} and liposomes ~~liposome~~ and make the mixing of cosmetics ~~mixing~~ more flexible and convenient.

The CoQ_{10}-containing preliposomes made according to the ~~by~~ present invention are a kind of solid preparation which are the granular and ~~lyophilized, before~~ lyophilized. Before using, water is added to the CoQ_{10}-containing ~~preliposomes, after~~ preliposomes. After hydration and surging, the CoQ_{10}-containing preliposomes ~~could~~ can become CoQ_{10}-containing liposomes.

The structure of the CoQ_{10}-containing preliposomes ~~mentioned in~~ of the present invention contain ~~contains~~ spongiamine ~~with the~~ at a concentration at 0.1% ~ 20% (W/W). Spongiamine can further facilitate the percutaneous absorption and improve the effect of CoQ_{10} in cosmetics. ~~the cosmetic.~~

The CoQ_{10}-containing preliposomes which contain spongiamine ~~mentioned in~~ according to the present invention are prepared by the following methods and processes. ~~method and process:~~

1) CoQ_{10}, spongiamine and other lipid ~~component~~ components are melted by heating or are dissolved by proper organic solvent(s) so that a ~~solvent, and~~ lipid solution is made,

2) ~~Use~~ A fluidized bed can be used to spray ~~bed, make~~ the above-mentioned lipid solution ~~sprayed~~ on ~~the~~ an underlay which is suspended in the middle of the fluidized ~~bed, let the~~ bed. The organic solvent is volatilized, and CoQ_{10}-containing preliposomes which contain spongiamine is obtained, ~~are got,~~

3) Make the lipid solution mentioned in step 1) and water solution which contains an underlay by known methods such as a membrane ~~disperse~~ dispersion method or a melt method or an infuse ~~method, and~~ method to obtain CoQ_{10}-containing liposomes which contain the underlay, ~~contains underlay aregot,~~

4) Make the CoQ_{10}-containing liposomes which contain an ~~contains~~ underlay by freeze drying or spray drying, or wiping ~~wipe~~ off the moisture to obtain ~~moisture,~~ CoQ_{10}-containing preliposomes which contains spongiamine. ~~spongiamine are got.~~

The CoQ_{10}-containing preliposomes ~~mentioned in~~ of the present invention ~~contains~~ contain CoQ_{10} ~~with the~~ at a concentration ~~at~~ of 0.2 ~ 40% (W/W). After ~~(W/W), after~~ restoring by adding water, the concentration of the CoQ_{10} is ~~at~~ 0.1 ~ 20% (W/W).

Suitable organic solvents that can be used according to the ~~The proper organic solvents mentioned in~~ present invention include dichloromethane, trichloromethane, ether and ethanol.

The concentration of underlay used according to the ~~mentioned in~~ present invention involved in the CoQ_{10} preliposomes which contain ~~contains~~ spongiamine is 1~80%.

Underlays that can be used according to the ~~The underlay mentioned in~~ present

invention ~~is~~ are selected from one of the following materials: mannitol, glucose, sorbitol, sucrose, lactose, fucose, sodium chloride and polyvinylpyrrolidone.

The lipid components that can be used according the ~~component mentioned in~~ present invention include spongiamine and at least one of the following components: cholesterol, soy lecithin, yolk lecithin, hydrogenated lecithin, DSPC, DPPP, poloxamer, DMPC and non-ionic surfactant like Brij.

The materials used ~~in~~ according to the present invention are all commercially available. ~~bought from the market.~~

The CoQ_{10}-containing preliposomes which contain ~~contains~~ spongiamine according to the ~~mentioned in~~ present invention not only have the same merit as the common ~~liposomes, for example,~~ liposomes in that they increase the stability of the ~~drug,~~ drugs, facilitate the percutaneous absorption of ~~the drug,~~ drugs, and prolong the time of drug ~~action, but also~~ action. In addition, the CoQ_{10}-containing preliposomes which contain spongiamine according to the present invention have the following merits:

1. The increased ~~Increase the~~ stability of CoQ_{10}-containing liposomes allow for longer storage times. ~~liposomes, can be stored for a long time.~~

Because the ~~above mentioned~~ the preliposomes are solid ~~drug, it can~~ drugs, they overcome the shortcomings that the common liposomes have, such as congregating, sedimentating, fusing, leaking ~~congregate, sedimentate, fuse,~~ and ~~leakage and~~ so on.

2. ~~Increase the~~ The stability of the CoQ_{10} is increased. ~~CoQ_{10}.~~

Because the ~~above mentioned~~ the preliposomes are solid ~~drug, it could~~ drugs, the present invention can be used to make ~~the~~ unstable ~~drug~~ drugs more stable in the solid state than in the liquid state.

3. ~~Facilitate the~~ The percutaneous absorption of the CoQ_{10} is increased. ~~CoQ_{10}.~~

~~Because the~~ The structure of the ~~above mentioned~~ liposomes ~~contain~~ containing spongiamine according to the present invention ~~spongiamine, it could obviously~~ facilitate the percutaneous absorption of drugs. ~~the drug~~.

4. ~~Can~~ The CoQ_{10}-containing liposomes of the present invention can be mixed with other components at ~~random; make it~~ at random making them easier and more convenient to formulate into cosmetics. ~~confect the cosmetic which contains CoQ_{10}.~~

Generally, for ~~the cosmetic~~ cosmetics which ~~contains liposome,~~ contain liposomes there is a certain range of the liposome volume. If the contains of liposomes exceed the range, ~~the character~~ characteristics of the cosmetics ~~cosmetic~~ will be affected, such as viscosity, flow property, viscosity, the content of the active component and so ~~on, furthermore,~~ on. Furthermore, certain cosmetics require different amounts of the CoQ_{10}. ~~it is different for the required content of CoQ_{10} for certain cosmetic.~~ Before use, water can be added to the CoQ_{10}-containing preliposomes which contain ~~contains~~ spongiamine according to the ~~mentioned in~~ present invention on demand, so as to provide liposomes which have different drug contents ~~content of drug can be got~~ to meet different cosmetic prescriptions.

~~prescription.~~

Examples

Example 1:

~~Get~~ In this example, 120g of CoQ_{10}, 50g of spongiamine, 50g of yolk lecithin, 100g of cholesterol, 100g of sucrose, were combined with enough ~~add~~ PBS (pH 7.4) to ~~the~~ produce a volume of 1000 ml.

~~Put~~ The CoQ_{10}, spongiamine, yolk lecithin and cholesterol from the above prescription were put into a triangle flask, ~~heat~~ heated to cause fusion, ~~store~~ and stored in a water bath at 80°C for further use. 800 ml of PBS (pH 7.4) was used to dissolve the ~~above mentioned~~ 140g of ~~sucrose, filter, heat the filter solution~~ sucrose. The dissolved solution was filtered and heated in a water bath to reach the same temperature with the ~~liposomes solution, mix the water~~ liposome solution. The sucrose solution was mixed with the liposome ~~liposomes~~ solution by surging and cooled. Enough ~~surging, then cool, add~~ PBS (pH 7.4) was added to ~~get~~ produce 1000 ml of the mixed ~~solution, after~~ solution. A high pressure homogeneous management (50 MPa of high pressure, 10 MPa of low ~~pressure),~~ pressure) was used to obtain a liposome ~~liposomes~~ suspension solution. ~~is got, after~~ After spray drying, a ~~kind of well~~ fluid CoQ_{10}-containing preliposomes which contained ~~contains~~ spongiamine was obtained. ~~is got~~.

Example 2:

~~Get~~ In this example, 30g of CoQ_{10}, 50g of spongiamine, 30g of soy lecithin, 100g of cholesterol, 40g of poloxamer F_{68}, 200g of glucose, and 200 ml of chloral, ~~add~~ were combined with enough PBS (pH 7.4) to ~~the~~ produce a volume of 1000 ml.

~~Put~~ The CoQ_{10}, spongiamine, soy lecithin, poloxamer F_{68} and cholesterol from the above prescription were put into a 1000 ml ~~ofrockered flask, use~~ rocked flask and the chloral was used to dissolve the lipid ~~components, rotary~~ components. The resulting mixture was subject to membrane ~~evaporate~~ evaporation in a water bath at 25~40°C to make the lipid form a membrane layer ~~of membrane~~ at the bottom of the rocked flask. ~~Rockered flask for further use.~~ ~~Use~~ 800 ml of PBS (pH 7.4) was used to dissolve the ~~above mentioned~~ 200g of glucose. The solution was filtered and added to the flask containing the lipid membrane for hydration thereof using surging. ~~glucose, filter, put the filter into the above mentioned flask, hydrating and surging, add~~ Enough PBS (pH 7.4) was added to produce ~~to get~~ 1000 ml of mixed ~~solution, after~~ solution which was subject to ultrasonic treatment (output 4, duty cycle 50%, time 10 ~~mins), liposomes~~ mins) to produce a liposome suspension solution. ~~is got, after~~ After freeze drying (temperature at -50°C the degree of vacuum is 50 millitorr), a kind of loose CoQ_{10}-containing preliposomes which contain ~~contains~~ spongiamine was obtained. ~~is got.~~

Example 3:

~~Get~~ In this example, 50g of CoQ_{10}, 50g of spongiamine, 60g of hydrogenated lecithin, 40g of cholesterol, 50g of poloxamer F_{68}, and 80g of fucose, 200ml of ether,

~~add~~ were combined with enough PBS (pH 7.4) to ~~the~~ produce a volume of 1000 ml.

~~Put~~ The CoQ_{10}, spongiamine, hydrogenated lecithin, poloxamer F_{68} and cholesterol from the above prescription were put into a 500ml of triangle ~~flask, use~~ flask and the ether was added to dissolve the lipid components for further use. ~~Use~~ 800 ml of PBS (pH 7.4) was used to dissolve the ~~above mentioned~~ 80g of ~~fucose, filter,~~ fucose. The fucose solution was filtered and put ~~the filter~~ into ~~a~~ the triangle ~~flask, store~~ flask which was stored in a water bath at 30~60°C, ~~mixing~~ and mixed round by magnetic force at the speed of 200~1000 ~~rpm, evaporate the organic solvent,~~ rpm. After the organic solvent was evaporation a liposome ~~liposomes~~ suspension solution was obtained and freeze dried ~~is got, after freeze drying~~ (temperature at -50°C, the degree of vacuum is 50 ~~millitorr),~~ millitorr) to produce a kind of loose CoQ_{10}-containing preliposomes which ~~contains~~ contain spongiamine. ~~is got.~~

Example 4: test of stability

~~Put~~ Samples of the three ~~batch~~ batches of ~~containing spongiamine~~ CoQ_{10}-containing preliposomes which contain spongaimine and a common CoQ_{10}-containing liposomes (the liposomes suspension before drying) were stored separately ~~into the condition which is~~ at a temperature of 40°C and at a relative humidity level of 75%. ~~degree of humidity.~~ After 0, 1, 2 and 3 months, ~~use~~ High Performance Liquid Chromatography (HPLC) was used to test the content of CoQ_{10} in the preliposomes and the common ~~liposomes, use the~~ liposomes. The content of 0 month CoQ_{10} in the preliposomes and the common liposomes was used as ~~100%,~~ 100%

to compare the content of drug at other ~~time~~ times with the above mentioned content of CoQ_{10}, and calculate ~~get~~ the percent content of drug as the time goes by.

Table 1 lists the stability comparing ~~result~~ results of the content of CoQ_{10} in the preliposomes and the common liposomes.

Table 1

	The change percent of the content of CoQ_{10} (%)			
Time (mo)	0	1	2	3
Common liposomes	100.00	93.32	88.03	83.50
Preliposomes	100.00	99.86	99.53	98.76

The ~~result shows~~ results show that the content of the drug contained in the common liposomes decreased along with the time ~~obviously, however,~~ while the content of the drug contained in the preliposomes ~~didn't decreased~~ did not decrease along with the time ~~significantly, it indicated~~ significantly. This indicates that the CoQ_{10}-containing preliposomes which ~~contains~~ contain spongiamine could evidently improve the stability of drugs. ~~the drug.~~